Prescrire's response to the public consultation on the document

"Risk proportionate approaches in clinical trials - Recommendations of the expert group on clinical trials for the implementation of
Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use"

Organising an institutional black out on adverse effects?

In this response we opt to comment exclusively on the « Safety reporting » section (4.2) to underline the shortcomings of this proposal, which is unacceptable both in practice and in principle.

We fully agree with lines 265-267 that state "*Detailed collection and reporting of adverse events (serious and non-serious) is particularly important where data about the safety profile of an IMP from available pre-clinical and clinical is scarce*". Yet, we strongly disagree with the sentences thereafter which include (267-274):

"*As the knowledge of a medicine and its use evolve and increasing amounts of data become available in order to determine the benefits and risks of an IMP, the level of detail and reporting requirements for adverse events may be adapted in the protocol, in line with the scope and type of a clinical trial and the level of knowledge on the safety profile of the IMP tested and the disease profile of the trial subjects.* ***This means in practice that the protocol may select only certain (and not all) adverse events to be recorded and reported to the sponsor. This applies in particular, <u>but not only</u>, to marketed products, with a known safety profile, which are tested within the framework of low-intervention clinical trials***."

This proposal is dangerous as it means that in practice clinical reports would not be complete and could become misleading, as they would be solely focused on efficacy in detriment of safety. How would it be possible to conduct an objective assessment of the harm-benefit ratio of the investigated medicinal product without having a full grasp of its safety profile? Such a plan to withhold data will bear further consequences: adverse effect data not being recorded in case report forms, new or secondary studies based on such selected safety data will also be biased; and adverse effect data not being reported to

pharmacovigilance authorities, these latest will not be able to carry out their work independently and reliably.

All in all, such a data destruction is in stark contrast with other provisions in the regulation which deal with transparency (see for instance R 536/2014 recitals 48, 51 and 67).

Another important concern with this proposal relates to the way scientists and health professionals tend to behave, and the confidence the public and patients are supposed to put in them.

Indeed, there is overwhelming evidence of under-reporting by health professionals of adverse drug reactions; and of bias in many clinical trials reports triggered by researchers and sponsors that privilege efficacy data collection over safety reporting, mainly due to commercial incentives. So if investigators and health professionals should ever be encouraged, this is to favour transparency and interest in adverse effects, not the reverse as this proposal does.

Patients need health professionals who take all adverse effects seriously. That means there should be no room to ignore, withhold or destroy data and that thorough collection and reporting of adverse effects must be upheld at all times and circumstances.